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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/922,200	09/02/97	KNUDSEN	L

HM11/1224

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EXAMINER	
MCKELVEY,T	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/24/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/922,200	Applicant(s) Knudsen et al.
	Examiner Terry A. McKelvey	Group Art Unit 1636

☒ Responsive to communication(s) filed on *10/19/98*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-34 and 39* is/are pending in the application.

Of the above, claim(s) *5, 7, 9, 11-19, 21-28, 32-34, and 39* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4, 6, 8, 10, 20, and 29-31* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

Applicant's election without traverse of the $CH_3(CH_2)_{10-24}CO$-NHCH(COOH)$(CH_2)_2CO$- lipophilic substituent, and GLP-2(1-33) species in Paper No. 8, filed 10/19/98 is acknowledged. The applicant indicated that the GLP-2(1-33) species reads on claims 29-32. This is incorrect for claim 32 because claim 32 is drawn to specific parent GLP2 peptides, none of which are just GLP-2(1-33).

Claims 5, 7, 9, 11-19, 21-28, 32-34, and 39 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected species. Election was made **without** traverse in Paper No. 8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 20 and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drucker et al (A) in view of Havelund et al (R).

Drucker et al teach GLP-2 derivatives and analogs, including GLP-2(1-33) (column 5; throughout the reference). This reference also teaches that the GLP-2 analogs can incorporate an amino acid substitution at one or more sites within a GLP-2 background, which is either a mammalian GLP-2 species (e.g., human) or a variant of a mammalian GLP-2 species in which the peptide has been modified to incorporate a blocking group of the type used conventionally in the art of peptide chemistry to protect the

peptide from undesired biochemical attack and degradation in vivo (columns 4, 5). GLP-2 and analogs of GLP-2 are taught as being useful for promoting the growth of small bowel tissue (column 2).

Drucker et al do not specifically teach the use of the elected species, $CH_3(CH_2)_{10-24}CO$-NHCH(COOH)$(CH_2)_2CO$-, as the substituent blocking group attached to GLP-2.

Havelund et al teach the use of a blocking group consisting of $CH_3(CH_2)_{12}CO$-NHCH(COOH)$(CH_2)_2CO$- attached to a protein, insulin, in order to stabilize the protein and increase the profile of action (Example 15; throughout the reference).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the blocking group taught by Havelund et al as a blocking group in making a GLP-2(1-33) analog having a blocking group as taught by Drucker et al because Drucker et al teach that it is within the ordinary skill in the art to use GLP-2(1-33) as a GLP-2 molecule and to add one or more blocking groups to the molecule, used conventionally in the art of peptide chemistry to protect peptides from undesired biochemical attack and degradation in vivo, and Havelund teaches many different blocking groups which function to stabilize proteins (i.e., has reduced degradation in vivo), such as the $CH_3(CH_2)_{12}CO$-NHCH(COOH)$(CH_2)_2CO$- substituent. One would have been

motivated to do so for the expected benefit of reducing the degradation of the resulting GLP-2 analog in vivo, resulting in protracted action, as taught by Havelund for proteins that contain the substituent, for a protein, a GLP-2 analog, which Drucker et al teach is useful for promoting the growth of small bowel tissue. Absent evidence to the contrary, there would have been a reasonable expectation of success that the GLP-2 analog resulting from the teachings of the combined references would be functional.

Claims 1-4, 6, 8, 10, 20, and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drucker et al (A) and Havelund et al (R) as applied to claims 1-4, 20 and 29-31 above, and further in view of Bodor (B).

Drucker et al and Havelund et al do not specifically teach attachment of the substituent by using an extra amino acid, or dipeptide.

Bodor teaches the use of an amino acid or dipeptide as a spacer inserted between the amino acid of a peptide and a bulky, lipophilic substituent which protects the peptide (abstract; throughout the reference).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use an extra amino acid or dipeptide to attach the substituent to the GLP-2 analog made obvious by the combined teachings of Drucker et al and Havelund et al because Bodor teaches that it is within the ordinary skill in the art to attach a bulky lipophilic substituent to a protein using an extra amino acid or dipeptide. One would have been motivated to do so for the expected benefit of proving a spacer between the bulky lipophilic group and the protein to which it becomes attached, as taught by Bodor, therefore more easily attaching the substituent to the protein because of a reduction of steric hindrance problems which could otherwise interfere with the attachment. Absent evidence to the contrary, there would have been a reasonable expectation of success that the resulting GLP-2 analog made from the combined teachings of the cited references would be functional.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December

28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (703) 305-7213. The examiner can normally be reached on Monday through Thursday from about 7:30 AM to about 5:00 PM. A phone message left at this number will be responded to as soon as possible (usually no later than 24 hours after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott, can be reached on (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Terry A. McKelvey

Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

December 23, 1998